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TOLERANCE AND RESPONSE OF SOMATOSTATIN ANALOGUE (SMS) SANDOSTATIN® FOR THE TREATMENT OF CHEMOTHERAPY INDUCED DIARRHEA. N. Petrelli, P. Creaven, L. Herrera, Y. Rustum, Roswell Park Cancer Institute, Buffalo, NY

Six patients (pts) developed severe diarrhea (4 or more loose watery stools per day requiring intravenous hydration) secondary to chemotherapy. All had failed treatment with lomotil®. Mean number of loose stools per day was 6 (range 4-16). All pts had tissue documented metastatic colorectal adenocarcinoma. There were 5 females and one male. Median age was 58 years (range 41-71). Chemotherapy consisted of weekly 5-Fluorouracil (5-FU) 600-750 mg/m^2 with 6S-leucovorin 250 mg/m^2 in 4 pts; 5-FU 500 mg/m^2 with 6R,S-leucovorin 500 mg/m^2 in one pt and one pt treated with oral Uracil and Ftorafur (UFT) 1200 mg/m^2 weekly. Sites of metastases were lung - 3 pts, liver - 2 pts, inguinal region - 1 patient. ECOG performance status was 0-1. Within 48 hrs of reporting diarrhea all pts were treated with intravenous fluid hydration, nothing by mouth and SMS. The latter was given to each pt in the following escalating doses: A continuous intravenous infusion of 50 micrograms (ug)/hour (h) for 12 h then 100 ug/h for 12 h then 150 ug/h for 72 h. Diarrhea completely resolved in 4 of 5 pts within 24 h of the 150 ug/h infusion. In the 6th pt the diarrhea resolved within 12 h of the 100 ug/h infusion. No side effects from SMS were seen. All pts resumed a regular diet without recurrence of the diarrhea. 150 ug/h has been an effective and safe schedule of SMS for the treatment of chemotherapy induced diarrhea. Pt accrual continues.

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THE COMBINED EFFECTS OF 5-FLUOROURACIL AND RECOMBINANT INTERFERON-GAMMA ON HUMAN GASTRIC CARCINOMA CELL LINES.

J.-G. Park, H.T. Kim, S.H. Park, N.K. Kim
Seoul National University Hospital, Seoul 110-744, KOREA.

Stomach cancer is a leading malignant disease in many countries. Conventional combination chemotherapy approaches to advanced gastric cancer only produce partial response and there has been no impact on patient survival from these approaches. Of several promising new approaches the combination of interferon and chemotherapeutic agents are now being made to improve the effectiveness for the treatment of cancer.

This study was conducted to investigate the combined effects of 5-FU and recombinant IFN-gamma at cellular level against four gastric carcinoma cell lines (SNU-1, SNU-5, SNU-16, and NCI-N87). We used a semiautomated tetrazolium-based colorimetric (MTT) assay for cytotoxicity and an isobologram analysis to evaluate the effects of combination. The experiment was performed three times on each of the three cell lines. Only two experiments for SNU-16 and NCI-N87 showed supraadditivity ($P < 0.02$). On isobologram plotted by the mean value of three experiments for each cell line, supraadditivity was suggested for only SNU-16 ($P=0.055$). In conclusion, our result did not document in vitro synergy between 5-FU and IFN-gamma for gastric carcinoma cell lines but additivity within clinically achievable dose range. Because in vivo immunomodulatory effect of IFN-gamma on host is more important rather than antiproliferative effect, the combination of 5-FU and IFN-gamma is expected to improve the treatment of advanced gastric cancer.

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HIGH DOSE AMINOTHIODIAZOLE (ATDA) IN ADVANCED COLORECTAL ADENOCARCINOMA: AN ILLINOIS CANCER COUNCIL (ICC) PHASE II STUDY. G. Locker, L. Kilton, J. Khandekar, D. Shevrin, K. Albain, R. Blough, A. Watkins, D. Tuteur. Illinois Cancer Council, Chicago, IL 60603.

Because previous Phase II studies of ATDA in advanced colon cancer employed drug doses less than maximally tolerated (MTD) and the suggestion of a dose response phenomenon of the drug against large bowel carcinomas (PROC ASCO: 113, 1989) the ICC conducted a Phase II study of ATDA at MTD. 30 patients with pathologically proven measurable recurrent or metastatic colorectal cancer were entered. 3 patients (pts.) had received radiosensitizing doses of 5-FU and radiation; 27 pts. had no prior chemotherapy. Median age was 64; 19 pts. were male; 11 female. 10 pts. were ECOG performance status (PS) 0; 20 were PS1. ATDA dose was 175 mg/M^2 IV weekly with escalation to 200 mg/M^2 if no toxicity seen. All pts. received prophylactic allopurinol and non-steroidal anti-inflammatory drugs to prevent hyperuricemia and dose-limiting chest pain. 20 pts. are currently evaluable for response (2 refused follow-up measurements, 2 missing data, 6 too early) and 22 are evaluable for toxicity. 12 pts. had dose escalations. Nausea (59% of pts.); dermatitis (41%), anemia (41%), diarrhea (32%) and stomatitis (18%) were generally of mild to moderate severity. Despite prophylaxis, 3 pts. developed chest pain. There were no objective responses seen, although 12 pts. had periods of stability lasting 1 to 19 months. Median survival was 15 months. ATDA given at MTD did not result in significant tumor regressions in patients with advanced colorectal carcinoma. Survival was longer than expected in a predominantly symptomatic patient population.

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SENSITIVITY OF SURVIVAL PATTERNS AFTER AJCC 1988 STAGING OF ESOPHAGEAL CANCER. E. Watkins Jr., M.J. Krasna, F.H. Ellis, Jr., G.J. Headley, and K. Balpgh. Lahey Clinic, Burlington, MA, and New England Deaconess Hospital and Harvard Medical School, Boston, MA.

The 1988 TNM pathologic staging version of the American Joint Committee on Cancer (AJCC) was applied to 281 patients who underwent standard esophageal resection for cure or palliation between 1970 through 1987.

The table indicates adverse influence of nodal disease on median survival time (MST) and 5-year survival with approach to significance (IIA vs. IIB, P = 0.12). Comparison is confounded by the variation in classification of local invasion in the two groups. Nodal influence is also suggested in the IIIT4 groups comparing N0 and N1 status (P = 0.09).

Influence of local advanced disease is suggested in comparison of IIIT3N1 and IIIT4N1 MST and survival, which is without statistical significance (P = 0.28).

Power analysis indicates that fragmentation of even large study groups into 7 categories frequently results in statistically meaningless results in late survivor groups with small risk populations.

We are currently evaluating a modified version of the Skinner WNM staging plan to be presented. The WNM schema permits comparison of degrees of local and nodal involvement with a modest increase in staging fragmentation.

Stage	TNM	MST Mo. ± SE	Survival 5 years % ± SE	Logrank P*
I	T1N0M0	>49.9	—	—
IIA	T2,3N0M0	24.5 ± 10.6	37.5 ± 6.7	0.82
IIB	T1,2N1M0	18.0 ± 4.3	16.2 ± 8.1	0.12
IIIT3N1	T3N1M0	21.9 ± 3.5	15.2 ± 6.6	0.91
IIIT4N0	T4N0M0	26.5 ± 4.9	16.7 ± 10.6	0.83
IIIT4N1	T4N1M0	14.0 ± 0.9	12.7 ± 4.5	0.09
IV	TNM1	6.0 ± 1.4	0	0.0001

* Logrank P between successive stage distributions

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